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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/904,766	07/12/2001	Avi Ashkenazi	10466/70	4054

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EXAMINER

KEMMERER, ELIZABETH

ART UNIT	PAPER NUMBER
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1646

DATE MAILED: 08/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/904,766

Applicant(s)

ASHKENAZI ET AL.

Examiner

Elizabeth C. Kemmerer, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 May 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 44-46 and 49-52 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 44-46 and 49-52 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☐ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 12/12/03.
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments, And/Or Claims

The amendment of 21 May 2004 has been entered in full. Claims 1-43, 47 and 48 are canceled. Claims 44-46 and 49-52 are under examination.

The copy of the declaration of Dr. Ashkenazi (originally filed in 09/903925) submitted under 37 CFR § 1.132 has been entered.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Withdrawn Objections And/Or Rejections

The rejection of claims 44-46 and 49-52 under 35 U.S.C. § 102(b) as being anticipated by Wood et al. (WO 99/14328) as set forth at p. 8 of the previous Office Action (mailed 21 January 2004) is *withdrawn* upon further consideration.

The rejection of claims 44-46 and 49-52 under 35 U.S.C. § 102(b) as being anticipated by Valenzuela et al. (WO 00/11015) as set forth at p. 9 of the previous Office Action (mailed 21 January 2004) is *withdrawn* upon further consideration.

Certificate of Correction

Applicant indicates (p. 4, Response of 21 May 2004) that they have not yet received a corrected filing receipt. The examiner has again requested that the Office of Initial Patent Examining issue a corrected filing receipt, reflecting the

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change in inventorship. If Applicant does not receive a corrected filing receipt, Applicant is invited to contact the examiner by phone to resolve the issue.

35 U.S.C. §§ 101 and 112, First Paragraph

Claims 44-46 and 49-52 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility.

Claims 44-46 and 49-52 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

The bases for these rejections are of record, for example, at pp. 4-7 of the previous Office Action (mailed 21 January 2004).

Applicant's arguments (pp. 4-9, Response of 21 May 2004) have been fully considered but are not found to be persuasive for the following reasons. The Ashkenazi declaration under 37 CFR 1.132 filed 21 May 2004 is insufficient to overcome the rejection of claims 44-46 and 49-52 based upon 35 U.S.C. §§ 101 and 112, first paragraph, as set forth in the last Office action for the following reasons.

Applicant reviews the evidentiary standard regarding the legal presumption of utility. Applicant argues that the USPTO has not met its burden of overcoming the presumption of the truth of an asserted utility. This has been

fully considered but is not found to be persuasive. The examiner takes no issue with Applicant's discussion of the evidentiary standard regarding the legal presumption of utility. Furthermore, the rejection does not question the presumption of truth, or credibility, of the asserted utility. The asserted utilities of cancer diagnostics and cancer therapeutics for the claimed proteins are credible and specific. However, they are not substantial. The data set forth in the specification are preliminary at best. As the courts have discussed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sup. Ct, 1966), an asserted utility must exist in currently available form. The specification indicates that the PRO269 gene is amplified in certain cancers. However, the literature reports that gene amplification does not necessarily result in increased expression at the mRNA and protein levels. See Pennica et al., Konopka et al., Haynes et al., cited in the previous Office Action.

Applicant urges that the USPTO has not made a *prima facie* case of lack of utility, in that Pennica et al. does not establish a lack of correlation between gene amplification and mRNA expression, and that Konopka et al. is limited to the *abl* gene, which is not recited in the claims. Applicant also criticizes Haynes et al. as being directed to yeast proteins rather than human proteins, and proteins that were highly abundant and not necessarily important regulatory proteins. Applicant also criticizes Haynes et al. for not addressing overexpression in tumor cells. Applicant takes issue with the conclusion that increased copy number may not result in increased protein expression, urging that the standard is not absolute certainty. Applicant argues that the WISP-2 or

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abl genes may be discrepancies. Applicant asserts that the working hypothesis among those skilled in the art is that, if a gene is amplified in cancer, the encoded protein is likely to be expressed at an elevated level. This has been fully considered but is not found to be persuasive. Regarding Pennica et al., the WISP-2 gene was still amplified as it was part of the amplicon tested.

Furthermore, Pennica et al. used a WISP-2 specific probe to test for amplification. Although Pennica et al. raise a question regarding the mechanism of the amplification, it is not relevant to the issue at hand since the WISP-2 gene was amplified without a corresponding increase in gene expression. Konopka et al. is relevant in spite of its being directed to a different gene, since it provides an example of an instance wherein a gene is amplified in a tumor whereas there is no corresponding increase in protein expression. Finally, Haynes et al. is relevant in that it studies eukaryotic gene expression, and finds that elevated mRNA levels do not correlate with elevated protein levels. The examiner agrees with Applicant's statement that absolute certainty is not the legal standard for utility. However, once again, the credibility of the assertion of utility is not questioned. The asserted utility is not substantial. The literature evidences that gene amplification does not reliably correlate with increased mRNA or protein expression. Therefore, further research would be required by the skilled artisan to determine if the disclosed results regarding a gene amplification event in tumors is also reflected at the mRNA and protein levels. The gene amplification data are preliminary with respect to whether or not the claimed protein can be used as a cancer diagnostic. Since the asserted utility that the claimed

polypeptides can be used to as cancer diagnostics is not in currently available form, the asserted utility is not substantial.

Applicant argues that even if a *prima facie* case of lack of utility has been established, it should be withdrawn on consideration of the totality of the evidence. Specifically, Applicant refers to the Ashkenazi declaration filed under 37 CFR § 1.132 with the amendment. The declaration and arguments assert that, even when amplification of a gene in a tumor does not correlate with an increase I protein expression, the absence of the gene product over-expression still provides significant information for cancer diagnosis and treatment. This has been fully considered but is not found to be persuasive. The examiner agrees that evidence regarding lack of over-expression would also be useful; unfortunately, there is no evidence as to whether the gene products (such as the protein) are over-expressed or not. Further research is required to determine such. Thus, the asserted utility is not present in currently available form, and is not substantial.

Applicant provides evidence in the form of a publication by Hanna et al., attached to the amendment. Applicant urges that the publication evidences that the HER-2/neu gene is over-expressed in breast cancers, and teaches that diagnosis of breast cancer includes testing both the amplification of the HER-2/neu gene as well as over-expression of the HER-2/neu gene product. Applicant argues that the disclosed assay leads to a more accurate classification of the cancer and a more effective treatment of it. The examiner agrees. In fact, Hanna et al. supports the rejection, in that Hanna et al. show that gene

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amplification does not reliably correlate with protein over-expression, and thus the level of protein expression must be tested empirically. The specification does not provide this further information, and thus the skilled artisan must perform additional experiments. Since the asserted utility for the claimed proteins is not in currently available form, the asserted utility is not substantial.

For all of these reasons, the rejection is maintained.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth C. Kemmerer, Ph.D. whose telephone number is (571) 272-0874. The examiner can normally be reached on Monday through Thursday, 7:00 a.m. to 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback, Ph.D. can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



ECK

ELIZABETH KEMMERER
PRIMARY EXAMINER